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REMARKS

This is a full and timely response to the final Office Action mailed December 28, 2007. Reconsideration of the application and allowance of presently pending claims as amended, are respectfully requested.

A. Present Status of Patent Application

Independent claims 38 and 54 have been directly amended, and the remaining claims indirectly amended as they depend from one of the amended Independent claims. Claim 103 is amended to correct a dependency. Claims 1-22, 40, 43, 45-46, 57, 59, 61 and 69-83 have been cancelled without prejudice, waiver or estoppel. Claims 23-37 and 84-102 had been previously withdrawn pursuant to a Restriction Requirement. New claims 104-106 have been added. Support for the new claims is found at least in paragraphs 0006, 0010-0011 and 0042-0043 of the specification.

Claims 38-39, 41-42, 44, 47-56, 58, 60, 62-68, and 103-106 remain pending.

B. Response to Rejections

1. Provisional Double Patenting Rejection

Applicant again notes the rejection of claims 1-8, 12-15, 19, 20, 38-44, 46-49, 52, 69-75, 77-79, and 82 on the ground of nonstatutory obviousness-type double patenting over the claims of co-pending U.S. application 11/187,757, and again notes the **provisional** status of the rejection. To the extent the provisional rejection matures into a double-patenting rejection which is the sole ground of rejecting the present claims, consideration will be given to filing the appropriate terminal disclaimer.

2. Rejection under 35 U.S.C. §112, Second Paragraph

Claims 16, 17, 50 and 51 were rejected under 35 U.S.C. §112 (second paragraph) as allegedly indefinite. Claims 16 and 17 have been cancelled, obviating the rejection thereto. The rejection is respectfully traversed as to the pending claims.

With reference to claim 50, it was contended that it conflicts with claim 38 in that the recitation of a "propellant" in claim 50 impermissibly extends the scope of the particulates. This rejection is traversed because there is no hierarchical error in the claims or in the claim language which could render the claim or claims indefinite. Independent claim 38 recites, in pertinent part:

> A pharmaceutical formulation for pulmonary administration, the pharmaceutical formulation comprising:...

and

> porous particulates consisting essentially of active agent particles in a matrix comprising a phospholipid, the active agent particles having a geometric diameter of less than about 3 μm and a solubility in water of about 0.1 to about 1.0 mg/ml and wherein the active agent particles are dispersed within the phospholipid matrix; and
> ...

The pharmaceutical formulation thus is **fully open ended as it comprises** the subsequently listed components. The **particulates are a subset of the formulation** and are claimed to be **less open ended** as "consisting essentially of." Claims 50 and 51, which depend from claim 38, do not purport to modify the particulates – they modify the **open ended formulation.** With regard to claim 50, the state of the particulates being suspended in a propellant in no way affects the nature of the formulation. With regard to claim 51, the state of the particulates being suspended in a liquid in no way affects the nature of the formulation. In both cases, the claiming hierarchy is thus preserved. Moreover, claim 38 does not specifically limit to a powder formulation, thus suspending the particulates in a liquid for aerosolization is technically sound and logically consistent.

3. Rejection under 35 U.S.C. §103(a)

Claims 1-22, 38-42, 44, 47-56, 58, 60, 62-68 and 103 were rejected under 35 USC §103(a) over *Weers et al.* WO 01/85136 or US 2002/0037316. The rejection is respectfully traversed as to the pending claims.

Weers et al is directed generally to a different type of composition, *to wit* a soluble or relatively soluble particulate formulation which is formulated from a solution of the soluble particle and the lipid. The particulate is designed to be aerodynamically light for effective delivery of active to the deep lung.

Thus as taught by *Weers et al:*

> Particularly preferred embodiments of the invention incorporate spray dried, hollow and porous particulate compositions as disclosed in WO 99/16419, hereby incorporated in its entirety by reference. Such particulate compositions comprise particles having a relatively thin porous wall defining a large internal void, although, other void containing or perforated structures are contemplated as well. In preferred embodiments the particulate compositions will further comprise an active agent.

Paragraph 0048.

> Whatever components are selected, the first step in particulate production typically comprises feed stock preparation. If the phospholipid based particle is intended to act as a carrier for another active agent, **the selected active agent is dissolved in a solvent, preferably water, to produce a concentrated solution.** *[emphasis added]*

Paragraph 0062.

In contrast, the invention of the applicants herein comprises a formulation and process to make an be aerodynamically light particulate formulation for effective delivery of active to the deep lung, however the active in the present invention is relatively insoluble and/or has a low T_g, as recited in Independent claims 38, 54 and 104.

The advantages of applicants' claimed invention are taught by the published specification of the present application:

> The pharmaceutical formulation comprises an active agent that is poorly water-soluble....It has been **unexpectedly discovered that active agents with a water solubility of from 0.1 mg/ml to 1.0 mg/ml can be effectively formulated.** This is unexpected in view of Lifshitz-Slezov-Wagner theory which predicts that active agents with a solubility in the range of 0.1-1.0 mg/ml would suffer from Ostwald ripening under a wide range of processing conditions generally used to produce aerosolizable pharmaceutical formulations.

Paragraph 0042.

> The dilemma facing formulators is that when the active agent has a low Tg, the amount of stabilizing excipient required may be large. This effectively limits the dose of active agent that can be practically delivered.

Paragraph 0010.

> ...Hence, excipients would be required to make up a large percentage of the dose, further limiting the dose that can be delivered. Hence, a need exists for the efficient and reproducible pulmonary delivery of drugs that have water solubilities less than 1 mg/ml.

Paragraph 0011

> Therefore, it is desirable to be able to produce a pharmaceutical formulation comprising an insoluble active agent. It is further desirable to produce the pharmaceutical formulation comprising an insoluble active agent in an economic, reproducible, and highly loaded manner. It is further desirable to produce an inhaleable pharmaceutical formulation comprising an insoluble active agent that may be effectively aerosolized and delivered to the lungs of a user.

Paragraph 0012

The dilemma facing formulators of the art when attempting to make aerodynamically light particles with low solubility, or low T_g, or both actives, was the need to use relatively large amounts of excipients. This effectively dilutes the active content, with concomitant need to deliver more of the formulation. Such a result is problematic when delivering powders pulmonarily, as there is a practical limitation on inspiration, thus forcing multiple doses.

Weers et al. does refer, in Example V, to powders which incorporate poorly soluble actives, but *Weers et al.* does not specifically teach or suggest the claimed compositions, and methods of making, comprising porous particulates **consisting essentially** of active agent particles in a matrix comprising a phospholipid, the active agent particles having a geometric diameter of less than about 3 μm and **a solubility in water of about 0.1 to about 1.0 mg/ml** and wherein the active agent particles are dispersed within the phospholipid matrix. Example V of *Weers et al.* incorporates an excipient (lactose monohydrate) thus teaching the opposite of the invention claimed by the applicants.

Weers et al. does not specifically teach or suggest a solution to the problem solved by the applicant herein.

As the independent claims are allowable over the prior art of record, then their dependent claims are allowable as a matter of law, because these dependent claims contain all features/elements/steps of their respective independent claim. *In re Fine*, 837 F.2d 1071 (Fed. Cir. 1988). Additionally and notwithstanding the foregoing reasons for the allowability of independent claims 38, 54 and 104, the dependent claims recite further features/steps and/or combinations of features/steps (as is apparent by examination of the claims themselves) that are patentably distinct from the prior art of record. Hence, there are other reasons why these dependent claims are allowable.

In view of the above, applicants respectfully request that these grounds of rejection be withdrawn.

Conclusion

In view of the foregoing, applicants submit that pending claims 38-39, 41-42, 44, 47-56, 58, 60, 62-68, and 103-106 satisfy the requirements of patentability and are therefore in condition for allowance. Reconsideration and withdrawal of all rejections is respectfully requested and a prompt mailing of a Notice of Allowance is solicited.

Please grant any extensions of time required to enter this response and charge any additional required fees to deposit account 50-0348.

If a telephone conference would expedite the prosecution of the subject application, the Examiner is requested to call the undersigned at (650) 283-6790.

Respectfully submitted,
Nektar Therapeutics

Date: 3/25/08

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